

AMENDMENT

1. (Original) A pharmaceutical composition comprising at least two compounds, one effecting opioid analgesia and one effecting local anesthesia, in amounts sufficient to potentiate an antinociceptive response when both compounds are topically administered in a physiologically acceptable topical excipient.

2. (Original) The topical pharmaceutical composition according to claim 1 comprising at least one analgesic and wherein the analgesic is selected from the group consisting of an opiate, an opiate derivative, an opioid, enkephalins, endorphins and synthetic opioid peptides.

3 (Original) The topical pharmaceutical composition according to claim 2, wherein the opioid is selected from the group consisting of ethylmorphine, hydromorphone, morphine, oxymorphone, codeine, levorphanol, oxycodone, pentazocine, propoxyphene, fentanyl, sufentanil, lofentanil, morphine-6-glucuronide and buprenorphine, methadone, etorphine, [D-Ala<sup>2</sup>,MePhe<sup>4</sup>,Gly(ol)<sup>5</sup>]enkephalin (DAMGO), butorphanol, nalorphine, nalbuphine, naloxone benzoylhydrazone,bremazocine, ethylketocyclazocine, U50,488, U69,593, spiradoline, naltrindole, [D-Pen<sup>2</sup>,D-Pen<sup>5</sup>]enkephalin (DPDPE), [D-Ala<sup>2</sup>,Glu<sup>4</sup>]deltorphan, and [D-Ser<sup>2</sup>,Leu<sup>5</sup>]enkephalin-Thr<sup>6</sup> (DSLET).

4. (Original) The topical pharmaceutical composition according to claim 2, wherein the enkephalin is selected from the group consisting of [D-Ala<sup>2</sup>, MePhe<sup>4</sup>, Gly(ol)<sup>5</sup>]enkephalin, Met-enkephalin, Leu-enkephalin and endomorphins.

5. (Original) The topical pharmaceutical composition according to claim 2, wherein the endorphin is selected from the group consisting of  $\beta$ -endorphin, dynorphin A, dynorphin B and  $\alpha$ -neoendorphin.

6. (Original) The topical pharmaceutical composition according to claim 1, wherein the analgesic is morphine.

7. (Original) The topical pharmaceutical composition according to claim 1, wherein the local anesthetic is selected from the group consisting of lidocaine, bupivacaine, mepivacaine, ropivacaine, tetracaine, etidocaine, chloroprocaine, prilocaine, procaine, benzocaine, dibucaine, dyclonine hydrochloride, pramoxine hydrochloride, benzocaine, and proparacaine.

8. (Original) The topical pharmaceutical composition according to claim 1, wherein the analgesic is morphine and the local anesthetic is lidocaine.

9. (Original) The topical pharmaceutical composition according to claim 1, wherein the local anesthetic is lidocaine.

10. (Original) The topical pharmaceutical composition according to claim 1 further comprising a tolerance attenuating or preventing NMDA receptor antagonist and wherein the NMDA receptor antagonist is selected from the group consisting of dextromethorphan, dextrophan, ketamine, pyroloquinoline quinone, cis-4-(phosphonomethyl)-2-piperidine carboxylic acid, MK801, memantine, and their mixtures and physiologically acceptable salts thereof.

11. (Original) A method of providing topical analgesia to a subject comprising topical administration of a pharmaceutical composition comprising at least two compounds, one effecting opioid analgesia and one effecting local anesthesia, wherein the pharmaceutical composition is administered in a physiologically acceptable topical excipient and in an amount and a duration sufficient to potentiate an antinociceptive response.

12. (Original) The method according to claim 11, wherein the analgesic is selected from the group consisting of an opiate, an opiate derivative, an opioid, enkephalins and endorphins.

13. (Original) The method according to claim 11, wherein the opioid is selected from the group consisting of ethylmorphine, hydromorphone, morphine, oxymorphone, codeine, levorphanol, oxycodone, pentazocine, propoxyphene, fentanyl, sufentanil, lofentanil, morphine-6-glucuronide and buprenorphine, methadone, etorphine, [D-Ala<sup>2</sup>,MePhe<sup>4</sup>,Gly(ol)<sup>5</sup>]enkephalin (DAMGO), butorphanol, nalorphine, nalbuphine, naloxone benzoylhydrazone, bremazocine,

ethylketocyclazocine, U50,488, U69,593, spiradoline, naltrindole, [D-Pen<sup>2</sup>,D-Pen<sup>5</sup>]enkephalin (DPDPE), [D-Ala<sup>2</sup>,Glu<sup>4</sup>]deltorphan, and [D-Ser<sup>2</sup>,Leu<sup>5</sup>]enkephalin-Thr<sup>6</sup> (DSLET).

14. (Original) The method according to claim 11, wherein the enkephalin is selected from the group consisting of [D-Ala<sup>2</sup>, MePhe<sup>4</sup>, Gly (ol)<sup>5</sup>] enkephalin, and endorphines.

15. (Original) The method according to claim 11, wherein the endorphin is selected from the group consisting of  $\beta$ -endorphin, dynorphin A, dynorphin B and  $\alpha$ -neoendorphin.

16. (Original) The method according to claim 11, wherein the analgesic is administered in a dose of about 0.01% to about 25%.

17. (Original) The method according to claim 11, wherein the analgesic is administered in a dose of about 0.1% to about 10%.

18. (Original) The method according to claim 11, wherein the analgesic is administered in a dose of about 0.5% to about 5%.

19. (Original) The method according to claim 11, wherein the analgesic is administered in a dose of about 0.01% to about 1%.

20. (Original) The method according to claim 11, wherein the analgesic is administered in a dose of about 0.01% to about 0.05%.

21. (Amended) The method according to claim 11, wherein the local anesthetic is selected from the group consisting of lidocaine, bupivacaine, mepivacaine, ropivacaine, tetracaine, etidocaine, chloroprocaine, prilocaine, procaine, benzocaine, dibucaine, dyclonine hydrochloride, pramoxine hydrochloride, benzocaine, butamben and proparacaine.

22. (Original) The method according to claim 11, wherein the local anesthetic is administered in a dose of about 0.01% to about 25%.

23. (Original) The method according to claim 11, wherein the local anesthetic is administered in a dose of about 0.1% to about 15%.

24. (Original) The method according to claim 11, wherein the local anesthetic is administered in a dose of about 0.5% to about 5%.

25. (Original) The method according to claim 11, wherein the local anesthetic is administered in a dose of about 0.01% to about 1%.

26. (Original) The method according to claim 11, wherein the local anesthetic is administered in a dose of about 0.01% to about 0.05%.

27. (Original) The method according to claim 11, wherein the pharmaceutical composition further comprises a tolerance attenuating or preventing NMDA receptor antagonist and where in the NMDA receptor antagonist is selected from the group consisting of dextromethorphan, dextrorphan, ketamine, pyroloquinoline quinone, cis-4-(phosphonomethyl)-2-piperidine carboxylic acid, MK801, memantine, and their mixtures and pharmaceutically acceptable salts thereof.

28. (Original) The method according to claim 11, wherein the NMDA receptor antagonist is administered in a dose of about 0.01% to about 25%.

29. (Original) The method according to claim 11, wherein the NMDA receptor antagonist is administered in a dose of about 0.1% to about 15%.

30. (Original) The method according to claim 11, wherein the NMDA receptor antagonist is administered in a dose of about 0.5% to about 5%.

31. (Original) The method according to claim 11, wherein the NMDA receptor antagonist is administered in a dose of about 0.01% to about 1%.

32. (Original) The method according to claim 11, wherein the NMDA receptor antagonist is administered in a dose of about 0.01% to about 0.05%.

33. (Original) The method according to claim 11, wherein topical administration of the pharmaceutical composition is directed to cutaneous, mucosal, vaginal, rectal, ocular, or nasal surfaces.

34. (Original) The method according to claim 11, wherein the pharmaceutical composition is topically administered to a subject in an amount and duration sufficient to prevent or relieve acute and chronic peripheral neuropathy.

35. (Original) The method according to claim 11, wherein the pharmaceutical composition is topically administered to a subject in an amount and duration sufficient to prevent or relieve neuropathic inflammation.